

### **REMARKS**

This Response is in reply to the Office Action mailed on June 2, 2006. Claims 1-3 and 5-7 are pending and claims 1 and 5 have been amended herein. Claim 4 has been cancelled. No new matter has been added. Entry and consideration of the amendments and following remarks is respectfully requested.

### **AMENDMENTS TO CLAIM 1**

Claim 1 has been amended to include the subject matter of cancelled claim 4. Further support for this amendment can be found in the specification on page 6, lines 4-11. No new matter has been added. In view of the incorporation of claim 4 into claim 1, the claim was amended to overcome the Examiner's objection to claims 4 and 5 under 35 U.S.C. § 112, second paragraph.

### **REJECTION UNDER 35 U.S.C. § 103(a)**

Claims stand rejected as obvious over Jozsef Neu et al. (WO 2004/026845), alone, or in view of David Sawyer (EP 0247892).

Amended claim 1 requires that once the reaction between 2,3-dichlorobenzoyl cyanide and aminoguanidine bicarbonate is complete, water is added and the pH of the medium is adjusted until the pH is higher than that of the pKa of hydrogen cyanide. Adjusting the pH ensures that the traces of hydrogen cyanide that are produced as a byproduct of the reaction are neutralized. This ensures that the filtering and isolation process, which is the next step in the method, results in a high purity and high yield. Furthermore, the isolation of intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile is advantageous because it allows a

highly pure lamotrigine to be obtained without the need of recrystallization. The ability to avoid one or more process steps of recrystallization following the cyclization step greatly improves the purity and the yield of the product.

In contradistinction, the Neu reference teaches away from isolating intermediate adduct of formula (IV) (of Neu) from the reaction medium. Instead of isolation, Neu teaches using magnesium oxide (See Neu, p. 2, line 31 and p. 4, line 7). Neu specifically states (p. 3, lines 11-18), "[t]herefore the object of the invention is a new process for the synthesis of high purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine of formula (I), using 2,3-dichlorobenzoyl cyanide as starting material and reacting it with the new dimesylate salt of aminoguanidine of formula (III) in the presence of methanesulfonic acid, then transforming the obtained adduct of formula (IV) **without isolation** into lamotrigine **with magnesium oxide**. In given case the so obtained crude **lamotrigine is recrystallized** from acetone using charcoal as clarifier" (emphasis added). The claimed invention obtains a high purity and yield without the use of magnesium oxide. Clearly, Neu cannot make obvious the claimed invention since it teaches away from the claimed process.

The claimed invention is further distinguished from Neu, because the claimed invention avoids recrystallization following the cyclization step. In stark contrast to the claimed invention, Neu specifically teaches that lamotrigine should be obtained by recrystallization (see the quoted passage above). Not only does Neu not teach or suggest the claimed invention, but its teachings contradict and teach away from the claimed invention. Accordingly, the rejection over Neu alone should be withdrawn. Furthermore, in view of the fact that Neu teaches away from the claimed invention, its use as a primary reference in a 103(a) rejection is untenable.

The Sawyer reference also fails to teach or suggest the claimed invention. As with the Neu reference, the Sawyer reference teaches one or more steps of recrystallization. In fact, the Sawyer reference was distinguished on these grounds in the background section of the present application (p. 4, lines 4-14). Requiring one or more steps of recrystallization, as Sawyer and Neu both do, results in significant disadvantages. For example, one or more steps of recrystallization will result in substantial yield losses. Accordingly, neither reference, either alone or in combination, teaches or suggests the claimed invention. It is respectfully submitted that the rejection be withdrawn and the application put into condition for allowance.


**CONCLUSION**

In view of the amendments to claims 1 and 5 made herein and the arguments presented above, it is submitted that the Examiner's rejections have been overcome and should be withdrawn. The application should now be in condition for allowance.

Should any changes to the claims and/or specification be deemed necessary to place the application in condition for allowance, the Examiner is respectfully requested to contact the undersigned to discuss the same.

This Response is being filed with a petition for a one-month extension of time and the required fee. In the event that any other extensions and/or fees are required for the entry of this Amendment, the Patent and Trademark Office is specifically authorized to charge such fee to Deposit Account No. 23-2820 in the name of Wolf, Block, Schorr & Solis-Cohen LLP. An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,  
WOLF, BLOCK, SCHORR & SOLIS-COHEN  
LLP.

By:   
Noam R. Pollack  
Reg. No. 56,829

Wolf, Block, Schorr & Solis-Cohen LLP  
250 Park Avenue, 10th Floor  
New York, New York 10177  
(212) 986-1116